

**REMARKS**

**A. Status of the Claims**

By the present amendment, claims 67, 73, 88-91, and 107-109 have been amended to more particularly define the Applicant's invention and to claim it with greater specificity. New claims 111-180 have been added. Claims amendments and new claims are supported by the specification and the original claims. No new matter has been added.

The Applicant acknowledges that in view of the amendment filed January 29, 2007, the previous rejections, i.e., the rejections under 35 U.S.C. § 103(a) over Page et al. in view of Overland et al, have been withdrawn. The Applicant further acknowledges that the finality of the previous Office Action has been also withdrawn.

The Applicant observes that the current Office Action indicates that claims 95 and 110 are objected to by the Examiner (see, the summary page, item 7). However, upon careful examination of the Office Action, the Applicant has been unable to determine what the grounds for these objections are. In addition, the Office Action contains no rejection of claims 95 and 110.

It is respectfully represented that the text of the Office Action does not provide any explanation. Accordingly, the Applicant requests clarification as to the status of claims 95 and 110 to allow the Applicant to fully respond to the objections.

After the present amendment has been entered, claims 67, 70, 73-81, 84-91, and 95-180 will be under consideration.

**B. Rejections Under 35 U.S.C. § 102 (e)**

Claims 67, 70, 73-81, 84-89, 91, and 96-108 stand rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent No. 5,981,601 to Nagley et al. ("Nagley") (page 2, last paragraph of the Office Action). The rejection is respectfully traversed on the following grounds.

It is axiomatic that a valid rejection of a claim for anticipation by a reference requires that the reference explicitly or inherently describe all of the elements, limitations, and relationships recited in the claim. It is submitted that Nagley does not describe all the elements and limitations recited in each of claims 67 and 91.

Indeed, Nagley teaches methods only for the treatment of the following diseases: Lebers disease, hereditary optic neuropathy, encephalomyopathy lactic acidosis, stroke-like episodes, chronic progressive external ophthalmoplegia, Kearns-Sayre syndrome, Pearson's marrow/pancreas syndrome, various cardiomyopathies, Parkinson's Disease, Alzheimer's Disease as well as heart failure, stroke and diabetes (see, col. 8, line 65 through col. 9, line 8).

Nagley fails to explicitly teach or inherently describe any of the specific diseases recited in claims 67 and 91. The Applicant respectfully points out that "encephalomyopathy lactic acidosis" disclosed by Nagley (col. 8, line 67) is not the same disease as "encephalomyopathy" recited in claims 67 and 91, nor is "encephalomyopathy lactic acidosis" disclosed by Nagley the same disease as "renal tubular acidosis" recited in claims 67 and 91.

Indeed, "encephalomyopathy lactic acidosis" mentioned by Nagley can be distinguished from "encephalomyopathy" recited in claims 67 and 91. More specifically, the syndrome known as "mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes" (MELAS) is known as a condition that affects many of the body's systems,

particularly the brain, nervous system and muscles caused by the build-up of lactic acid and is typically characterized by the symptoms such as muscle weakness and pain, recurrent headaches, loss of appetite, vomiting, and seizures.

At the same time, "encephalomyopathy" is a broader term referring to any disease involving the brain and muscles, such as any of a group of diseases characterized by abnormal mitochondrial function with involvement of the central nervous system and skeletal muscle. While in many cases encephalomyopathy is associated with lactic acidosis, this is not always so. Thus, encephalomyopathy does not have to be MELAS syndrome, and can include, for example, subacute necrotizing encephalomyelitis or MERRF syndrome.

Therefore, Nagley fails to disclose every element of claims 67 and 91, and, therefore, is not a proper prior art reference under 35 U.S.C. § 102(e). Thus, each of claims 67 and 91 is patentably distinguishable over Nagley. Each of claims 70, 73-81, 84-89, and 96-108 directly or indirectly depends on either claim 67 or claim 91, and is accordingly considered patentable for at least the same reason. Withdrawal of the rejection and reconsideration are respectfully requested.

**C. Rejections Under 35 U.S.C. § 103 (a)**

Claims 67, 70, 73-81, 84-91, and 96-109 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious Nagley in view of Page et al., "Developmental Disorder Associated with Increased Cellular Nucleotidase Activity," *Proc. Natl. Acad. Sci. USA*, vol. 94, pp. 11601-11606 (1997) ("Page")(page 4, last paragraph of the Office Action). The rejection is respectfully traversed on the following grounds.

The standard that has to be satisfied in order to make a valid rejection based on a prima facie case of obviousness was described in a response to a previous Office Action. This standard has been modified recently by the recent Supreme Court decision in the

KSR International v. Teleflex Inc. (550 U.S. \_\_\_ (2007)), and there is no longer a strict requirement to satisfy the old “teaching-suggestion-motivation” standard to show obviousness. Under the KSR rule, three basic criteria are considered. First, some suggestion or motivation to modify a reference or to combine the teachings of multiple references still has to be shown. Second, the combination has to suggest a reasonable expectation of success. Third, the prior art reference or combination has to teach or suggest all of the recited claim limitations. Factors such as the general state of the art and common sense may be considered when determining the feasibility of modifying and/or combining references.

The Examiner has stated that Nagley discloses what is described above, but does not teach a particular dosage of 6 g/m<sup>2</sup> and uses the teaching of Page to cure this deficiency (see, page 5, first paragraph of the Office Action). While the Examiner is correct that Page teaches such dosages, the combination of references fails to teach or suggest all of the limitations recited in claims 67 and 91.

More specifically, as discussed above, Nagley fails to disclose or suggest any specific disease or condition recited in claims 67 and 91. Page likewise fails to either disclose or suggest any such diseases, only mentioning developmental delay, seizures, ataxia, infections, language deficit and behavioral problem. There is nothing in either reference or in combination thereof showing that the method can be used for treatment of any other diseases nor is there any reasonable expectation of success in doing so.

In view of the foregoing, it is respectfully submitted that each of claims 67 and 91 is patentably distinguishable over Nagley in view of Page. Each of claims 70, 73, 73-81, 84-90, and 96-109 depends, directly or indirectly, either on claim 67 or on claim 91, and is allowable for at least the same reason. Reconsideration and withdrawal of the rejection are respectfully requested.

**D. New Claims**

By the present amendment, the Applicant added new claims 111-180. These claims are both novel and non-obvious over the cited art. Indeed, each of claims 111-145 is directed to the methods that include administering a composition having **only** a compound of Formula (I) or (IA) as an active compound, as can be easily seen from the fact that the transitional clause "consisting of" has been employed in claims 111-145. Claims 111-145 **exclude using any other active compounds**.

To contrast, Nagley fails to disclose or suggest using a composition having a single active compound, and in fact **requires using a minimum of two** compounds (i.e., uridine or derivative plus a redox compound such as a benzoquinone derivative). Accordingly, Nagley teaches a different method.

With regard to new claims 146-180, the list of recited diseases in these claims does not include encephalomyopathy. Accordingly, claims 146-180 are somewhat narrower in scope than pending claims 67, 70, 73-81, 84-91, and 95-109, but are otherwise novel and non-obvious over Nagley for the same reasons as those discussed above.

In the Application of:  
Robert K. Naviaux  
Application Serial No.: 09/889,251  
Filed: November 1, 2001  
Page 26

PATENT  
Attorney Docket No.: UCSD1140-1

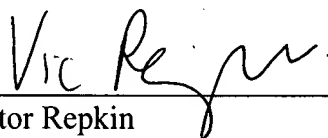
**CONCLUSION**

In view of the above amendments and remarks, reconsideration and favorable action on all claims are respectfully requested. In the event any matters remain to be resolved, the Examiner is requested to contact the undersigned at the telephone number given below so that a prompt disposition of this application can be achieved.

No fee is deemed necessary with the filing of this response. However if any fees are due, the Commissioner is hereby authorized to charge any fees, or make any credits, to Deposit Account No. 07-1896 referencing the above-identified attorney docket number. A copy of the Transmittal Sheet is enclosed.

Respectfully submitted,

Date: July 17, 2007

  
\_\_\_\_\_  
Victor Repkin  
Attorney for Applicants  
Registration No. 45,039  
Telephone: (858) 638-6664  
Facsimile: (858) 677-1465

DLA PIPER US LLP  
4365 Executive Drive, Suite 1100  
San Diego, California 92121-2133  
**USPTO CUSTOMER NUMBER 28213**